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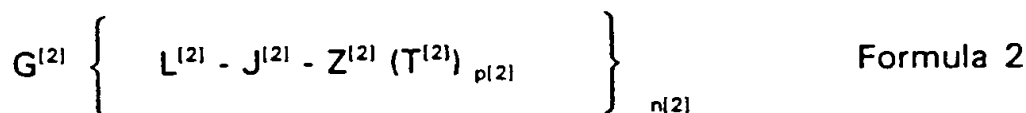
Claims

WE CLAIM:

1. A conjugate comprising (a) biological or
5 chemical molecules reacted with (b) a chemically-defined,
non-polymeric valency platform molecule of the formula:



or



wherein

each of $G^{[1]}$ and $G^{[2]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2000 chain atoms selected from the group C, N, O, Si, P and S;

each of the $n^{[1]}$ moieties shown as $T^{[1]}$ and each of the $p^{[2]} \times n^{[2]}$ moieties shown as $T^{[2]}$ is independently chosen from the group NHR^{SUB} (amine), $C(=O)NHNHR^{SUB}$ (hydrazide), $NHNHR^{SUB}$ (hydrazine), $C(=O)OH$ (carboxylic acid), $C(=O)OR^{ESTER}$ (activated ester), $C(=O)OC(=O)R^B$ (anhydride), $C(=O)X$ (acid halide), $S(=O)_2X$ (sulfonyl halide), $C(=NR^{SUB})OR^{SUB}$ (imidate ester), NCO (isocyanate), NCS (isothiocyanate), $OC(=O)X$ (haloformate), $C(=O)OC(=NR^{SUB})NHR^{SUB}$ (carbodiimide adduct), $C(=O)H$

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(aldehyde), $C(=O)R^B$ (ketone), SH (sulfhydryl or thiol), OH (alcohol), $C(=O)CH_2X$ (haloacetyl), $R^{ALK}X$ (alkyl halide), $S(=O)_2OR^{ALK}X$ (alkyl sulfonate), NR^1R^2 wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$ (maleimide), $C(=O)CR^B=CR^B_2$ (α,β -unsaturated carbonyl), $R^{ALK}-Hg-X$ (alkyl mercurial), and $S(=O)CR^B=CR^B_2$ (α,β -unsaturated sulfone);
 wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other good leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, pentafluorophenoxy, or other activating group;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

each of the $n^{[2]}$ moieties shown as $L^{[2]}$, if present, is independently chosen from the group O, NR^{SUB} and S;

each of the $n^{[2]}$ moieties shown as $J^{[2]}$, if present, is independently chosen from the group $C(=O)$ and $C(=S)$;

$n^{[1]} = 1$ to 32;

$n^{[2]} = 1$ to 32;

$p^{[2]} = 1$ to 8;

with the proviso that the product $n^{[2]} \times p^{[2]}$ be greater than 1 and less than 33;

each of the $n^{[2]}$ moieties shown as $Z^{[2]}$ is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, containing

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attachment sites for at least p²¹ functional groups on alkyl, alkenyl, or aromatic carbon atoms.

5 2. A conjugate according to claim 1, wherein the biological molecules comprise polynucleotide duplexes of at least about 20 base pairs each bound to the valency platform molecule, the duplexes each having a significant binding activity for human systemic lupus erythematosus
10 anti-dsDNA autoantibodies.

3. A conjugate according to claim 1, wherein the biological or chemical molecules are selected from the group consisting of carbohydrates, lipid,
15 lipopolysaccharides, peptides, proteins, glycoproteins, single-stranded or double-stranded oligonucleotides, haptens, or chemical analogs thereof such as mimotopes, aptamers.

20 4. A conjugate according to claim 1, wherein the biological or chemical molecules are analogs of immunogens wherein (a) the analog binds specifically to B cells to which the immunogen binds specifically and (b) the conjugate lacks a T cell epitope.

25 5. The conjugate of claim 1, wherein the valency platform molecule is derivatized by a reagent selected from the group consisting of DABA, BAHA, BAHA_α, and AHAB.

30 6. The conjugate of claim 2, wherein a linker molecule couples the duplexes to the valency platform molecule.

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7. The conjugate of claim 6, wherein the linker molecule is selected from the group consisting of HAD and HAD_pS.

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8. The conjugate of claim 2, wherein the duplexes are substantially homogeneous in length.

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9. The conjugate of claim 2, wherein the duplexes are substantially homogeneous in nucleotide composition.

10. The conjugate of claim 2, wherein the duplexes are 20 to 50 bp in length.

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11. The conjugate of claim 2, wherein the duplexes are bound to the valency platform molecule at or proximate one of their ends.

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12. The conjugate of claim 2, wherein the conjugate is a tolerogen for human systemic lupus erythematosus.

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13. A conjugate according to claim 2, wherein the polynucleotide duplexes have a B-DNA type helical structure and a significant binding activity for human systemic lupus erythematosus anti-dsDNA autoantibodies.

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14. A pharmaceutical composition for treating lupus comprising the conjugate of claim 2 formulated with a pharmaceutically acceptable injectable vehicle.

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15. A method for treating an individual for lupus comprising administering a therapeutically effective amount of the composition claim 14 to an individual in need of such treatment.

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16. A method for making the conjugate of claim 2, comprising:

5 (a) bonding a multiplicity of single-stranded polynucleotides of at least about 20 base pairs each on the valency platform molecule; and

10 (b) annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the valency platform molecule to form said duplexes.

15 17. A pharmaceutical composition for treating an antibody-mediated pathology comprising a therapeutically effective amount of the conjugate of claim 2, combined with a pharmaceutically acceptable carrier.

20 18. A method of inducing specific B cell anergy to an immunogen in an individual comprising administering to the individual an effective amount of the conjugate of claim 17.

25 19. A method of treating an individual for an antibody-mediated pathology in which undesired antibodies are produced in response to an immunogen comprising administering a therapeutically effective amount of the conjugate of claim 17 to the individual.

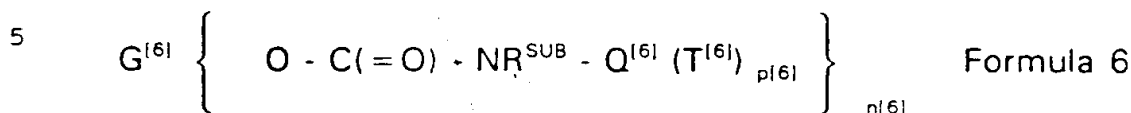
30 20. A method for making a conjugate according to claim 2, comprising

(a) covalently bonding the analog of the immunogen lacking T cell epitopes to the chemically-defined valency platform molecule to form a conjugate; and

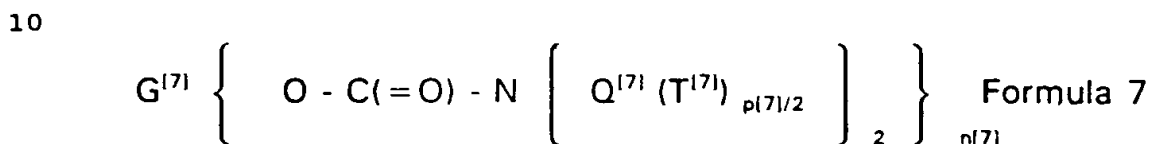
35 (b) recovering the conjugate from the reaction mixture.

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21. A chemically-defined, non-polymeric valency platform molecule of the formula:



or



wherein

each of $G^{[6]}$ and $G^{[7]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2000 chain atoms selected from the group C, N, O, Si, P and S;

each of the $n^{[6]} \times p^{[6]}$ moieties shown as $T^{[6]}$ and each of the $n^{[7]} \times p^{[7]}$ moieties shown as $T^{[7]}$ is independently chosen from the group

NHR^{SUB} (amine), $C(=O)NHNHR^{SUB}$ (hydrazide), $NHNHR^{SUB}$ (hydrazine), $C(=O)OH$ (carboxylic acid), $C(=O)OR^{ESTER}$ (activated ester), $C(=O)OC(=O)R^B$ (anhydride), $C(=O)X$ (acid halide), $S(=O)_2X$ (sulfonyl halide), $C(=NR^{SUB})OR^{SUB}$ (imide ester), NCO (isocyanate), NCS (isothiocyanate), $OC(=O)X$ (haloformate), $C(=O)OC(=NR^{SUB})NHR^{SUB}$ (carbodiimide adduct), $C(=O)H$ (aldehyde), $C(=O)R^B$ (ketone), SH (sulfhydryl or thiol), OH (alcohol), $C(=O)CH_2X$ (haloacetyl), $R^{ALK}X$ (alkyl halide), $S(=O)_2OR^{ALK}X$ (alkyl sulfonate), NR^1R^2 wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$ (maleimide), $C(=O)CR^B=CR^B_2$ (α,β -unsaturated carbonyl),

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$R^{ALK}-Hg-X$ (alkyl mercurial), and $S(=O)CR^B=CR^B_2$ (α,β -unsaturated sulfone);
wherein

5 each X is independently a halogen of atomic number greater than 16 and less than 54 or other good leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

10 each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, pentafluorophenoxy, or other activating group;

15 each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]} = 1$ to 32;

$p^{[6]} = 1$ to 8;

20 with the proviso that the product $n^{[6]} \times p^{[6]}$ be greater than 1 and less than 33;

$n^{[7]} = 1$ to 32;

$p^{[7]} = 2, 4, 6$ or 8;

with the proviso that the product $n^{[7]} \times p^{[7]}$ be greater than 1 and less than 33;

25 each of the $n^{[6]}$ moieties shown as $Q^{[6]}$ and each of the $2 \times n^{[7]}$ moieties shown as $Q^{[7]}$ is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, containing attachment sites for at least $p^{[6]}$ (for $Q^{[6]}$) or $p^{[7]}/2$ (for $Q^{[7]}$, where $p^{[7]}/2$ is an integer)
30 functional groups on alkyl, alkenyl, or aromatic carbon atoms.

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